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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/902,692	07/30/97	REA W	16715CIP

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TODD E ALBANESI
CRUTSINGER & BOOTH
1601 ELM STREET SUITE 1950
THANKSGIVING TOWER
DALLAS TX 75201-4744

EXAMINER	
SCHWADRON, R	

ART UNIT	PAPER NUMBER
1644	11

DATE MAILED: 02/12/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/902,692	Applicant(s) Rea et al.
	Examiner Ron Schwadron, Ph.D.	Group Art Unit 1644

☐ **Responsive** to communication(s) filed on _____.

☐ **This action is FINAL.**

☐ **Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.**

A shortened statutory period for response to this action is set to expire 3 **month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).**

Disposition of Claims

☒ Claim(s) *1-48* is/are pending in the application.

Of the above, claim(s) *8-19, 21, 32, and 40-48* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7, 20, 22-31, and 33-39* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ **See the** attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ **The drawing(s) filed on** _____ is/are objected to by the Examiner.

☐ **The proposed drawing correction, filed on** _____ is ☐ approved ☐ disapproved.

☐ **The specification is objected to by the Examiner.**

☐ **The oath or declaration is objected to by the Examiner.**

Priority under 35 U.S.C. § 119

☐ **Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).**

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ **Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).**

Attachment(s)

☒ **Notice of References Cited, PTO-892**

☒ **Information Disclosure Statement(s), PTO-1449, Paper No(s).** _____

☐ **Interview Summary, PTO-413**

☐ **Notice of Draftsperson's Patent Drawing Review, PTO-948**

☐ **Notice of Informal Patent Application, PTO-152**

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

15. Applicant's election with traverse of Group I, claims 1-7 and 20 in Paper No. 10 is acknowledged. Regarding applicants comments about amended claims 22 and 28 and Group II as enunciated in the previous Office Action, said group now reads on the invention of Group I and therefore Group I will now include claims 1-7,20,22-31,33-39. The traversal is on the ground(s) that are stated in said paper. Regarding applicants comments about Groups III and IV (as enunciated in the restriction requirement mailed 9/28/98), said arguments are not found persuasive because of the following reasons. Regarding applicants comments, the M.P.E.P. § 803 (July 1998) states that: "For purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The restriction requirement enunciated in the previous Office Action meets this criterion and therefore establishes that serious burden is placed on the Examiner by the searching of additional Groups III and IV. The requirement is still deemed proper and is therefore made FINAL.

16. Claims 8-19,21,32,40-48 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions, the requirement having been traversed in Paper No. 10.

17. Claims 1-7,20,22-31,33-39 are under consideration.

18. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because of the following reasons.

A) The instant application needs to claim priority to PCT/US96/01205 under 35 USC 120, not 35 USC 119 (see MPEP section 1895.01, page 1800-131). In addition, the first sentence of the specification indicates that priority is claimed as a CIP which could only be claimed under 35 USC 120.

B) The first paragraph of the specification indicates that priority is claimed to US application 08/380063. There is no priority claim to said application in the instant declaration. Priority to said application would be claimed under 35 USC 120 as a CIP. If applicant does not intend to claim

priority to US application 08/380063, then reference to said application needs to be deleted from the first paragraph of the specification (irregardless of whether said application is related to PCT/US96/01205) because reference to said application in the first paragraph of the specification indicates a claim of priority to said application.

C)It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

19. The use of the trademark FICOLL HYPAQUE and ISOLYMPH has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 1-7,20,22-31,33-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to use the claimed methods for the treatment of disease in vivo in humans. The claimed methods are drawn to methods of regulating an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said

method encompasses the in vivo treatment of humans. The specification has not provided evidence that the claimed invention can be used to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in vivo in humans. The claimed invention encompasses the treatment of cancer in vivo in humans (eg. wherein the continuously dividing T and B are tumor cells of T or B cell origin). The claimed invention encompasses the treatment of autoimmune disease in vivo in humans (eg. wherein the continuously dividing T and B lymphocytes provoke autoimmune disease). The claimed invention encompasses the treatment of HIV in vivo in humans (eg. wherein the continuously dividing T cells are HIV infected). The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the claimed methods is the in vivo treatment of disease in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence in humans to as to whether the claimed invention can be used to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of humans to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes and the in vivo treatment of cancer, autoimmune disease and HIV infection.

Regarding the use of the claimed method to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of humans, there is no evidence in the specification that such regulation has been achieved using the claimed method. The claimed method encompasses a method wherein the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal is normalized. The only actual data disclosed in the specification wherein the cell cycle of human cells is analyzed is that represented in Figures 2-4. Figures 2a and 2b represent data indicating the cell cycle of human peripheral T lymphocytes from "normal" volunteers. This data provides no information about the cell cycle of human peripheral B lymphocytes from "normal" volunteers. The claimed method recites that abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal is regulated. Figures 3a -3c purport to show the "irregular cell cycle profiles from environmentally compromised individuals". There is no disclosure as to what cells are referred to in said figure (eg. only T cells, T and B cells, unfractionated lymphocytes, unfractionated leukocytes, etc.). Thus, it is unclear if there is any relationship between the data disclosed in Figure 2 and that in Figure 3 because it is unclear whether said Figures refer to the

same or different cell populations. A similar problem exists with the data represented in Figure 4. Furthermore, if the data disclosed in Figure 4 refers to the cell cycle of T cells, it appears that the cell cycle of untreated patients in Figure 4a more closely approximates that seen in the normal controls than that seen in Figure 4c. Thus, the evidence of record suggests that the claimed method cannot be used to "regulate" the cell cycle of abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes because the term regulate would encompass normalization of an abnormal cell cycle and this has not been demonstrated. In addition, based on the data presented in the specification, it is unclear whether any effect on the cell cycle of continuously dividing B lymphocytes in a mammal has been achieved. Furthermore, regarding the data disclosed in Figure 4c, in the absence of appropriate control data (untreated patient) it is unclear whether the data presented represents a random fluctuation seen in patients unrelated to treatment. Regarding the use of the claimed invention to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein the mammal is a human infected with HIV, no data has been presented indicating that abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a such a patient has been modified. Regarding the single HIV positive patient described in the specification in page 22, no cell cycle data has been provided from said patient indicating that the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in said patient has been modified. Regarding any clinical observations seen in said patient, there is no description of what other medications said patient was taking so it is unclear whether the results disclosed in said example are related to ALF treatment or were related to some other treatment. Furthermore, there is no disclosure as to what the "ALF" used to treat said patient consisted of. It is unclear what "ALF" means or encompasses for the reasons addressed elsewhere in this Office Action. Regarding the treated cancer patients referred to in the specification, no cell cycle data has been provided from said patients indicating that the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in said patients has been modified. It is unclear as what treatment said patients were given in addition to ALF and if their disease was effected by ALF treatment. Furthermore, there is no disclosure as to what the "ALF" used to treat said patient consisted of. It is unclear what "ALF" means or encompasses for the reasons addressed elsewhere in this Office Action. There is also no evidence provided that the claimed invention can be used to regulate the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in patients suffering from autoimmune disease. Thus, based on the

disclosure in the specification, it is unclear as to whether the claimed invention can be used to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of humans and the in vivo treatment of cancer, autoimmune disease and HIV infection.

Regarding the method of claims of methods 1-7,20,28-31,33-39, said claims specify that the lysate is prepared from "normal lymphocyte blood cells from the mammal". However, none of the experiments disclosed in the specification are performed using such a lysate. The experiments disclosed in the specification use a lysate prepared from abnormal lymphocytes derived from the patient to whom the lysate will be administered (see page 9, especially lines 1-3). This is not the preparation recited in the claimed method. Furthermore, there is no disclosure in the specification as to how such a preparation could be made. There is no guidance in the specification as to how normal lymphocytes would be derived from an individual who by definition in the claim contains abnormal lymphocytes. Regarding claims 22-27, said claims recite the use of ALF. The specification appears to define ALF as "a substance derived from an individuals own normal T and B lymphocytes isolated from a blood sample" (see page 3). However, it appears that the experiments disclosed in the specification were performed using a preparation containing abnormal lymphocytes (eg. derived patients with abnormal lymphocytes, see page 9, especially lines 1-3), that by definition is not an ALF. There is no disclosure in the specification as how to produce ALF derived from autologous lymphocytes for use in the claimed method wherein normal lymphocytes are derived from an individual that has abnormal lymphocytes by definition in the claims. The claims as currently written also encompass the use of allogeneic blood cells, but there is no evidence of record that allogeneic cells can be used in the claimed method.

Regarding the use of the methods of the instant invention to treat HIV infection in vivo in humans, Fahey et al. teach that appropriate evidence is required in order to demonstrate that a particular agent can be used for the treatment of HIV infection in humans. No such evidence has been disclosed in the instant application and therefore it is unpredictable whether the method of the instant invention could be used to treat HIV infection in humans. Regarding the use of the methods of the instant invention to treat cancer in vivo in humans, Osband et al. teach that appropriate evidence is required in order to demonstrate that a particular agent can be used for the treatment of cancer in humans. No such evidence has been disclosed in the instant application and

therefore it is unpredictable whether the method of the instant invention could be used to treat cancer in humans. It appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

21. Claim 1-7,20,22-31,33-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1,22,28 are indefinite in the recitation of "regulating an abnormal lymphocytic cell cycle" because it is unclear what this means or encompasses. Claim 29 contains the trademark/trade name FICOLL-HYPAQUE. Claim 33 contains the trademark/trade name ISOLYMPH. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe and, accordingly, the identification/description is indefinite. Claims 22,23 are indefinite in the recitation of "ALF" because it is unclear what this term means or encompasses. The specification discloses on page 3, lines 7-9 that ALF is a "substance derived from an individuals own normal T and B lymphocytes isolated from a blood sample and then propagated in a cell culture". However, the specification describes on page 9 an "ALF" preparation made from an individuals own abnormal T and B lymphocytes because the individual used is described as having abnormal T and B cells. Thus, it is unclear what "ALF" means or encompasses. Furthermore, it is unclear what a "substance derived from an individuals own normal T and B lymphocytes" means or encompasses. It is unclear what the "substances" means or encompasses in the context of the definition of the term ALF. Thus, based on the indefinite and contradictory definitions of "ALF" in the specification, it is unclear as to what said term means or encompasses. Claim 1 is indefinite in the recitation of "normal lymphocyte blood cells" because it is unclear what this term means or encompasses. Claim 28 is indefinite in the

recitation of "normal lymphocytes of the blood" because it is unclear what this term means or encompasses. It is unclear as to what constitutes a normal lymphocyte. For example, the art recognizes that T cells which bind nominal antigen in the context of MHC can also bind bacterial superantigens. The T cell which binds nominal antigen in the context of MHC could be considered "normal" to the extent that said cell is not mediating a pathologic immune reaction. However, upon the introduction of bacterial superantigen such as TSST, said "normal T cell" can now interact with TSST to cause pathological phenomenon (eg. toxic shock syndrome mediated by TSST). It is unclear whether said T cell now is "normal" or "abnormal". The T cell is the same T cell irregardless of the antigen to which it is responding.

22. No claim is allowed.

23. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 305-3014.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644
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